NIEHS
National Institute of Environmental Health Sciences

Presidential Symposium AAAS Annual Meeting: Challenge from Risk-Risk Tradeoffs

February 18, 2006

David A. Schwartz, M.D.
Director
National Institute of Environmental Health Sciences

U.S. Department of Health and Human Services
National Institute of Health
National Institute of Environmental Health Services

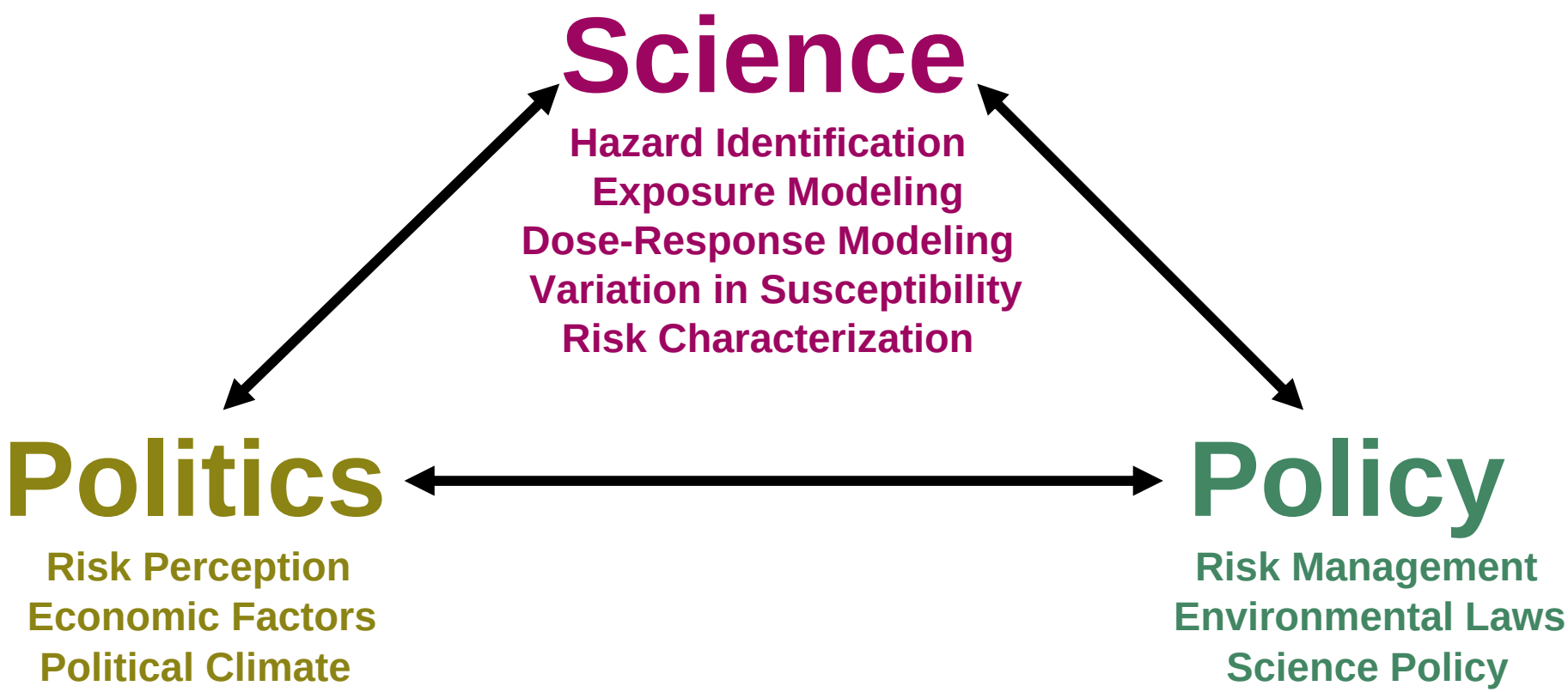
NIEHS
National Institute of Environmental Health Sciences

Science of Environmental Health

- Risk Assessment
- Relationship to NIEHS Strategic Plan
- Priorities for Program Development

U.S. Department of Health and Human Services
National Institute of Health
National Institute of Environmental Health Services

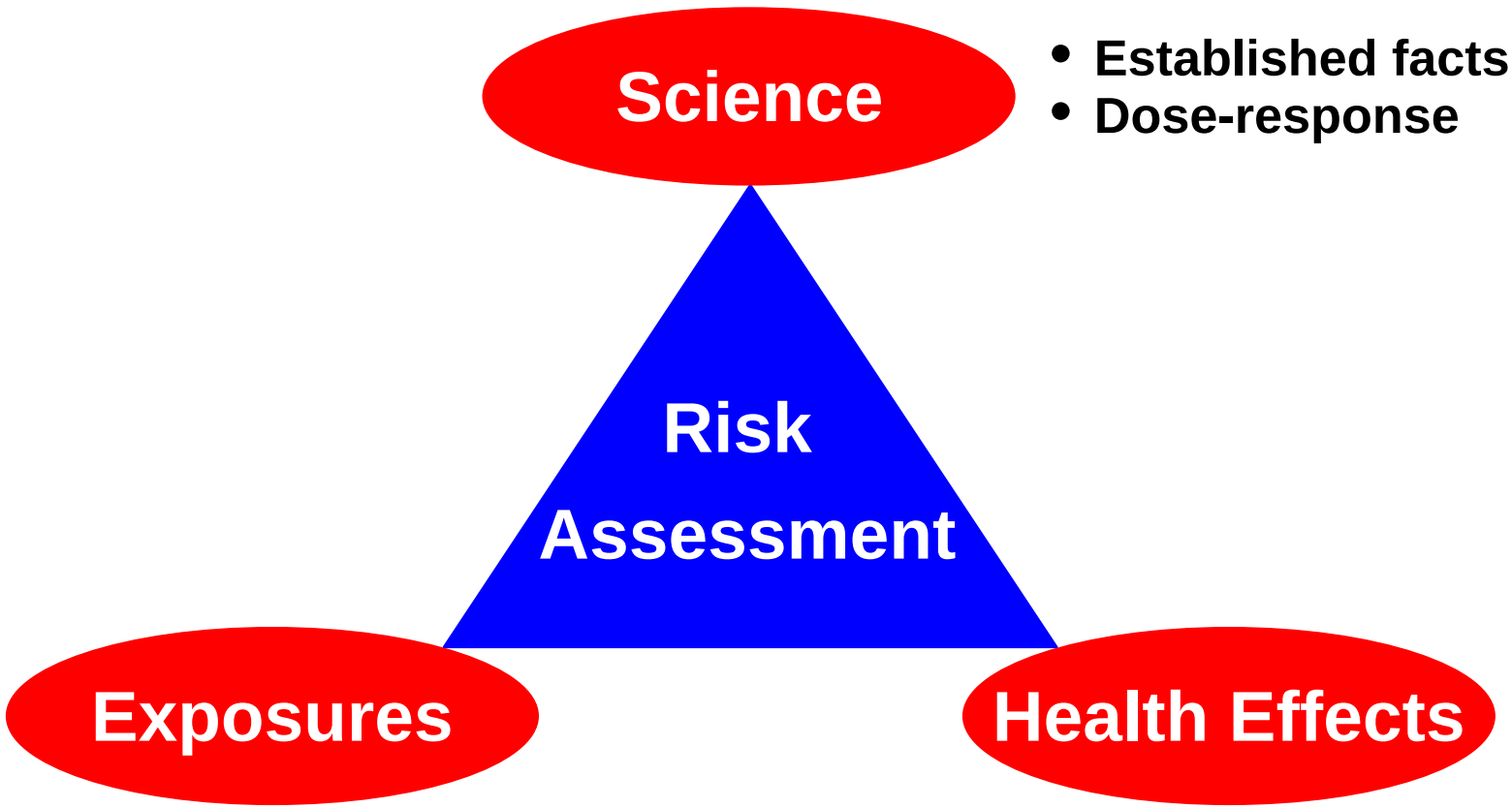
Decisions About Environmental Hazards



Decisions are made with relative, not absolute, certainty of knowledge

What is Risk Assessment?

National Academy of Sciences, 1983



- Established facts
- Dose-response

- New or existing agents and mixtures
- Potential for exposure

- Toxicity → Disease
- Susceptibility

Risk Assessment Methodology is Necessary

- All agents have the potential to cause harm
  - the critical question - to what degree?
- Risk (probabilistic) vs. hazard (inherent toxicity)
  - risk = probability of hazard under given conditions
- Without risk assessment…
  - no discussion of relative degree of harm from potentially toxic agents
  - no control over new agents

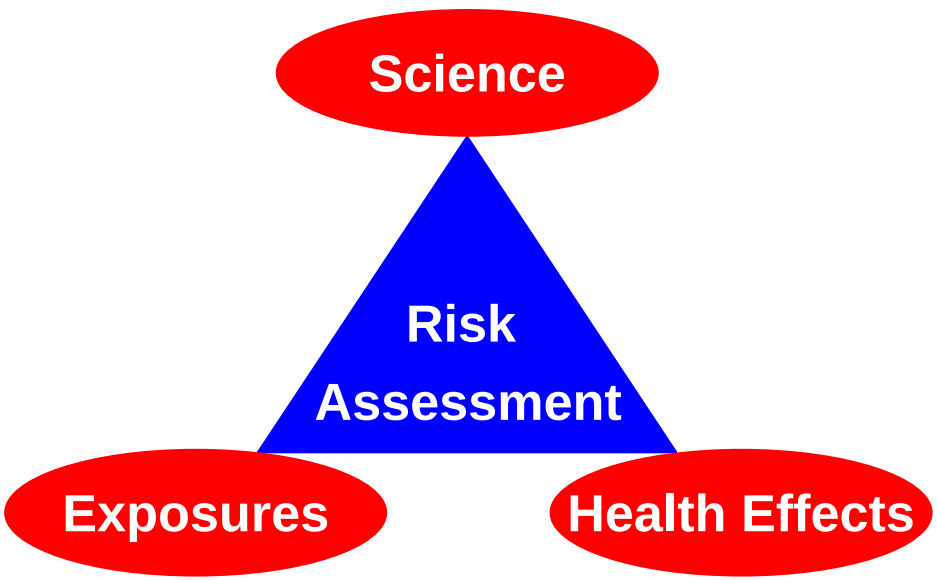
Risks:Risk Tradeoffs

[need to consider risk and exposed population]

- **Hazard - inherent toxicity of the agent**
- **Dose-Response**
  - **allows one to compare risk per unit dose**
- **Fully Characterized Risk**
  - **accounts for extent of exposure**
  - **“population attributable risk”**

	Dioxin	Di-Ethylhexyl Phthalate
Human Carcinogen	yes	reasonably anticipated
Dose – Response	0.2 ng	1 ng
Body Burden (U.S.A.)	very low	much higher

Risk – Risk Tradeoffs: Issues to Consider



- Who makes the comparison?
- Purpose of the comparison
- Limitations of the risk projections
- Relation and comparability to other risks under consideration
- Uncertainties in the risk predictions (hazards, dose-response, exposure, and differential susceptibility)

Role for Environmental Health Sciences

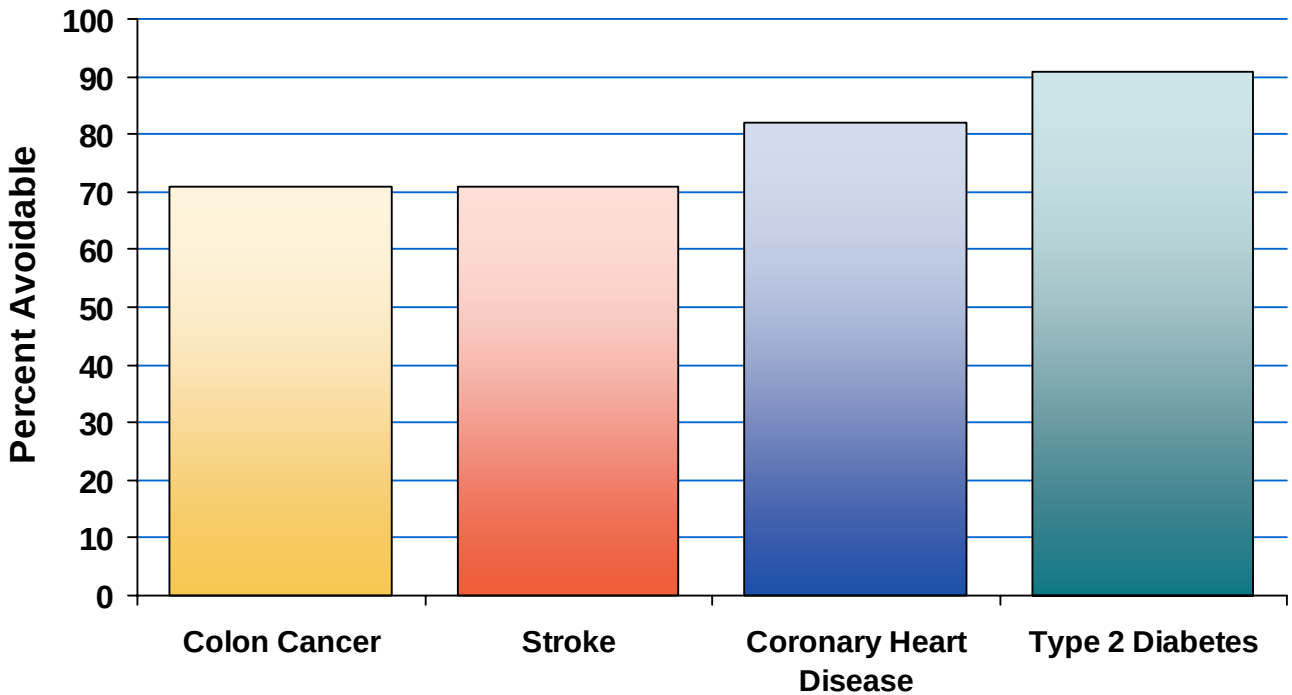
- **Improve strategies to identify toxicants of concern**
  - **Exploit comparative biology**
  - **Focus on common biological responses**
- **Develop a scientific basis for risk comparisons**
  - **Exposure sciences – toxicity, dose-response, and mechanisms**
  - **Extrapolation of model organisms to humans**
  - **Genetic susceptibility**
- **Improve intervention strategies**
  - **Classical regulation strategies**
  - **Clinical/population-based intervention strategies**

Vision for NIEHS

Use environmental sciences to understand human disease and improve human health

- Complex human diseases
- Exposure biology
- Global environmental health

Complex Human Diseases: Challenge and Opportunity

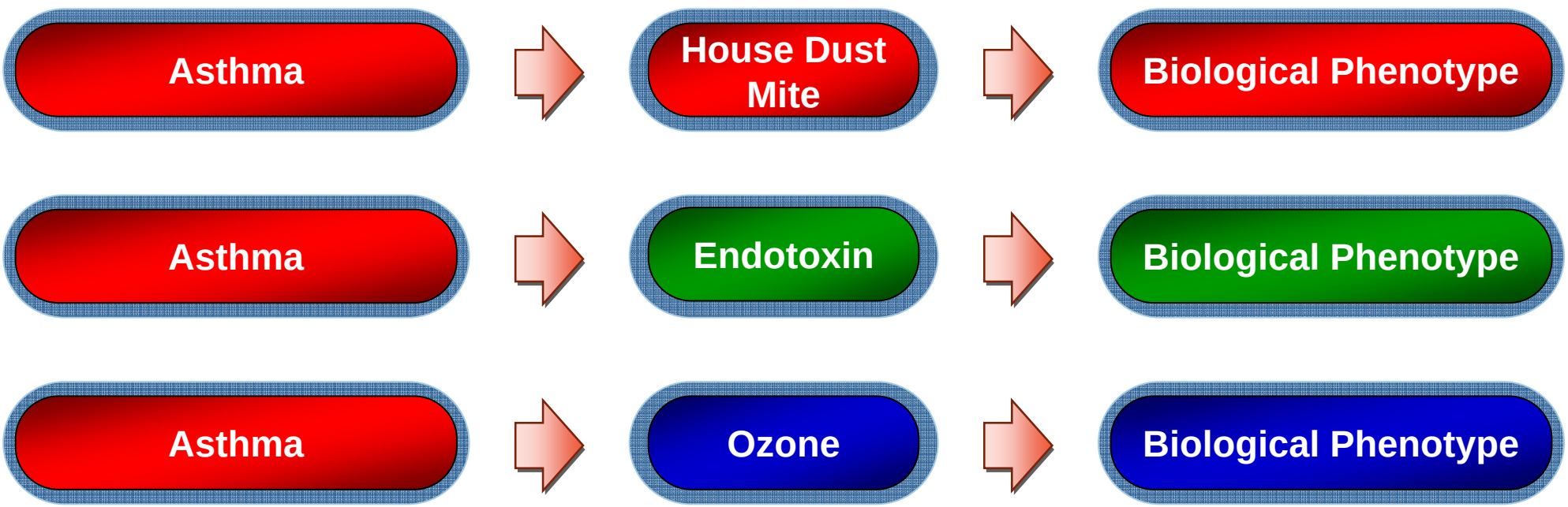


- 70-90% of the major diseases in the USA are caused by reversible behaviors and exposures
- Single gene mutations are the major cause of cancers and CVD in < 5% of the cases

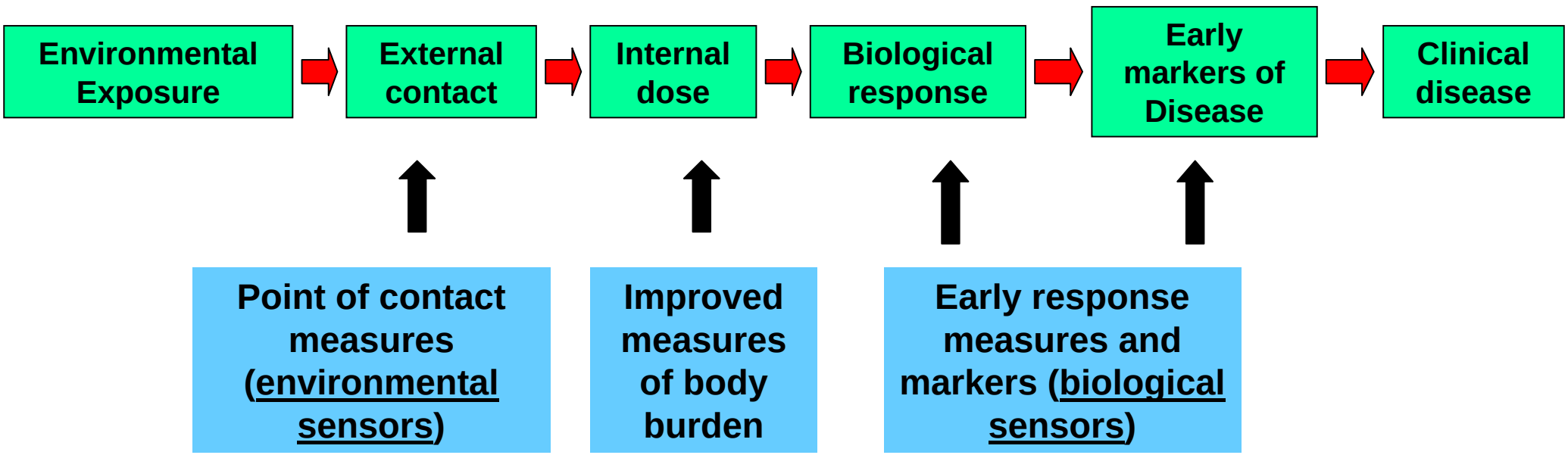
Willett. *Science* 2002; 296:695

Exposures Can Simplify Complex Diseases

Exposures Can Simplify Complex Diseases

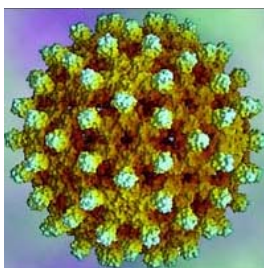


Infrastructure Needs: More Precise Markers of Exposure



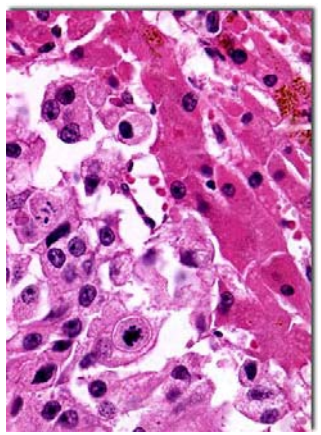
Links personal exposures to biological response

Etiology of Hepatocellular Carcinoma



HBsAg (serum)

Insertional Mutagensis → Chronic Inflammation → Cell Proliferation → Hepatitis Cirrhosis



Reactive Intermediates → Promutagenic DNA Lesions → P53 Mutations

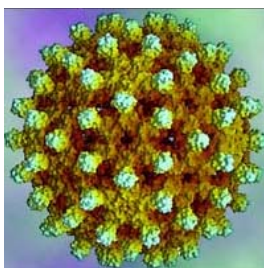
Aflatoxin Mercapturic Acid (urine)

Aflatoxin-N7-guanine (urine)

Arg249Ser Mutations (serum)

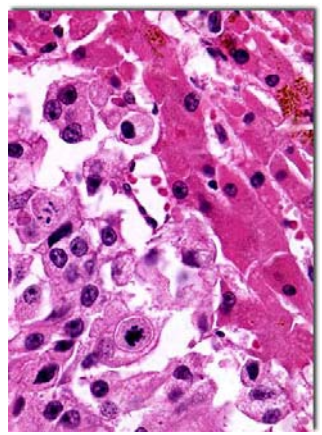
Etiology of Hepatocellular Carcinoma

No association between dietary aflatoxin and liver cancer



HBsAg (serum)

Insertional Mutagensis → **Chronic Inflammation** → **Cell Proliferation** → **Hepatitis Cirrhosis**



Reactive Intermediates → **Promutagenic DNA Lesions** → **P53 Mutations**

	Aflatoxin Mercapturic Acid (urine)	**Aflatoxin-N7-guanine (urine)**	**Arg249Ser Mutations (serum)**

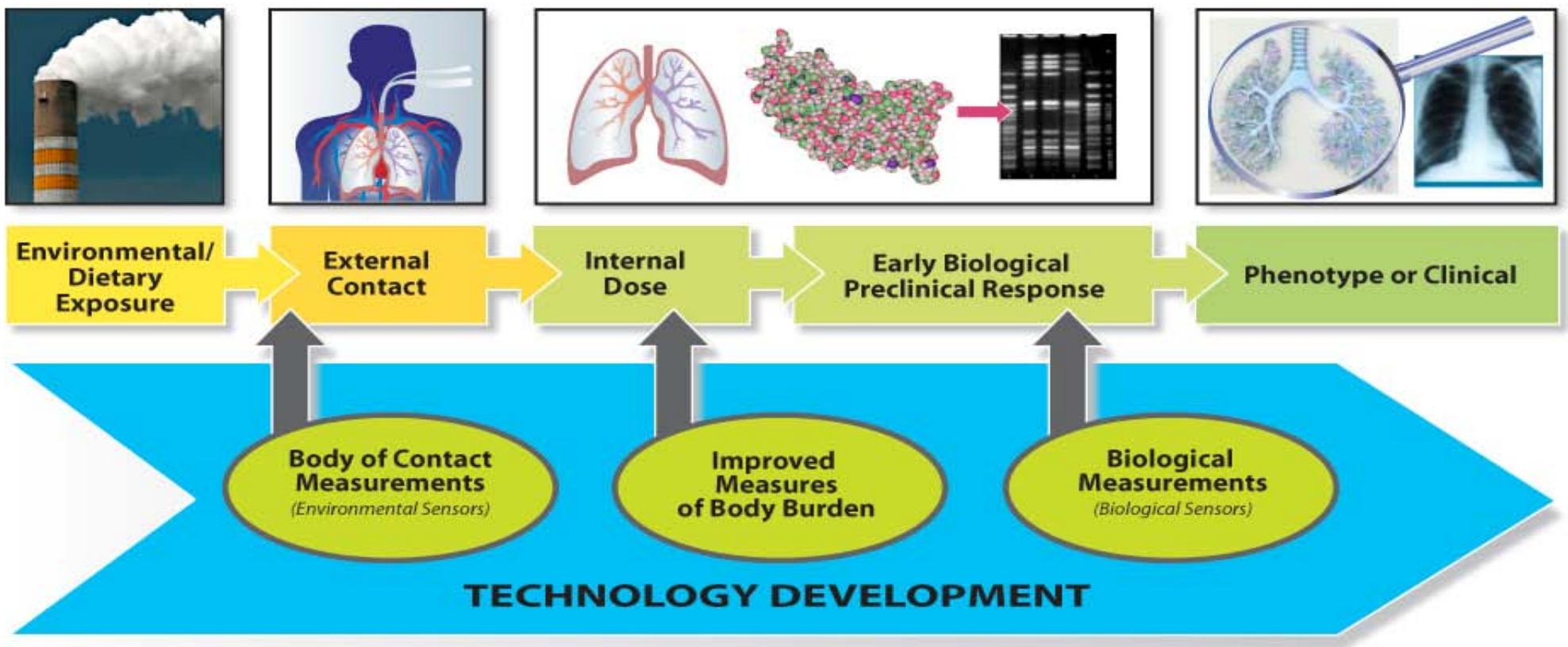
	RR
Aflatoxin	3.8
HBV	7.3
Aflatoxin + HBV	60.0

Genes and Environment Initiative (GEI)

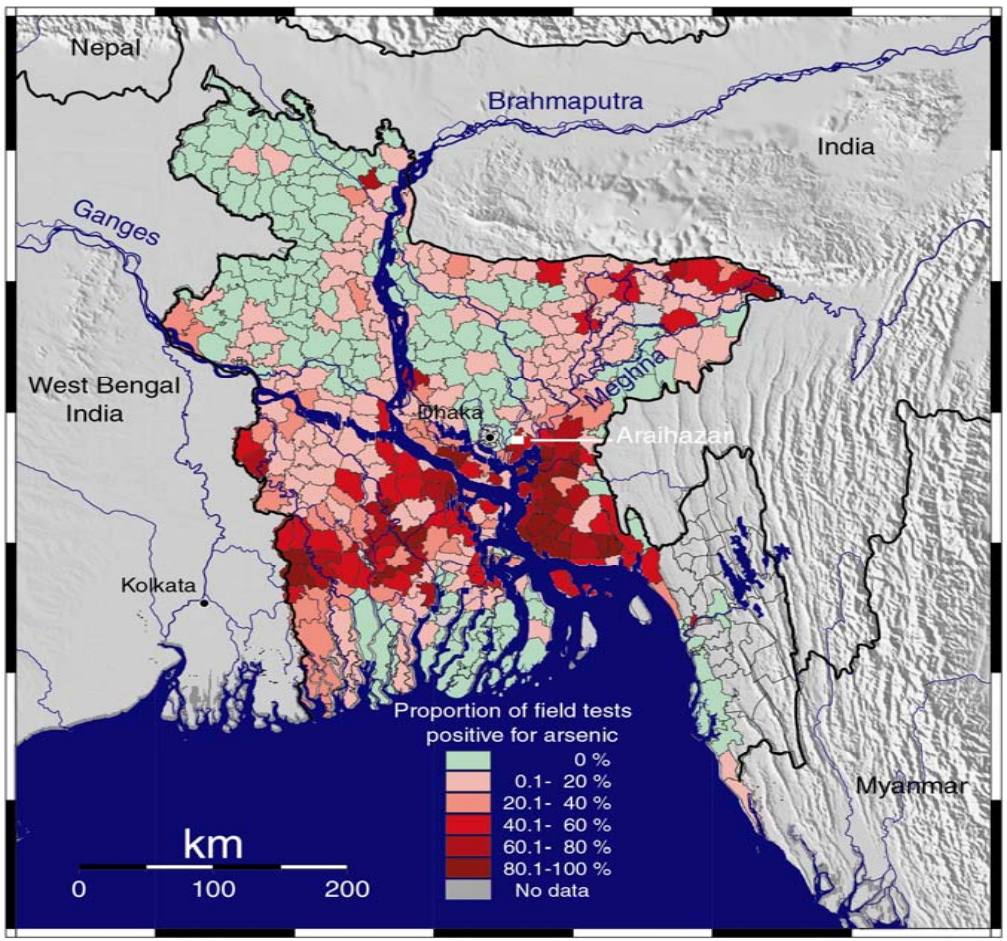
- **Secretarial Initiative in FY2007 President's Budget**
- **2007-2010: $40 million/yr**
  - **$26 million human genetic case-control studies (HapMap)**
  - **$14 million environmental biology program**
- **Environmental Biology Program – environment, diet, and activity level**
  - **Sensor technology**
  - **Biological response indicators**
  - **Workshop – Spring, 2006**

NIH coordinated
Centrally managed
Product oriented

Conceptual Approach to Environmental Biology



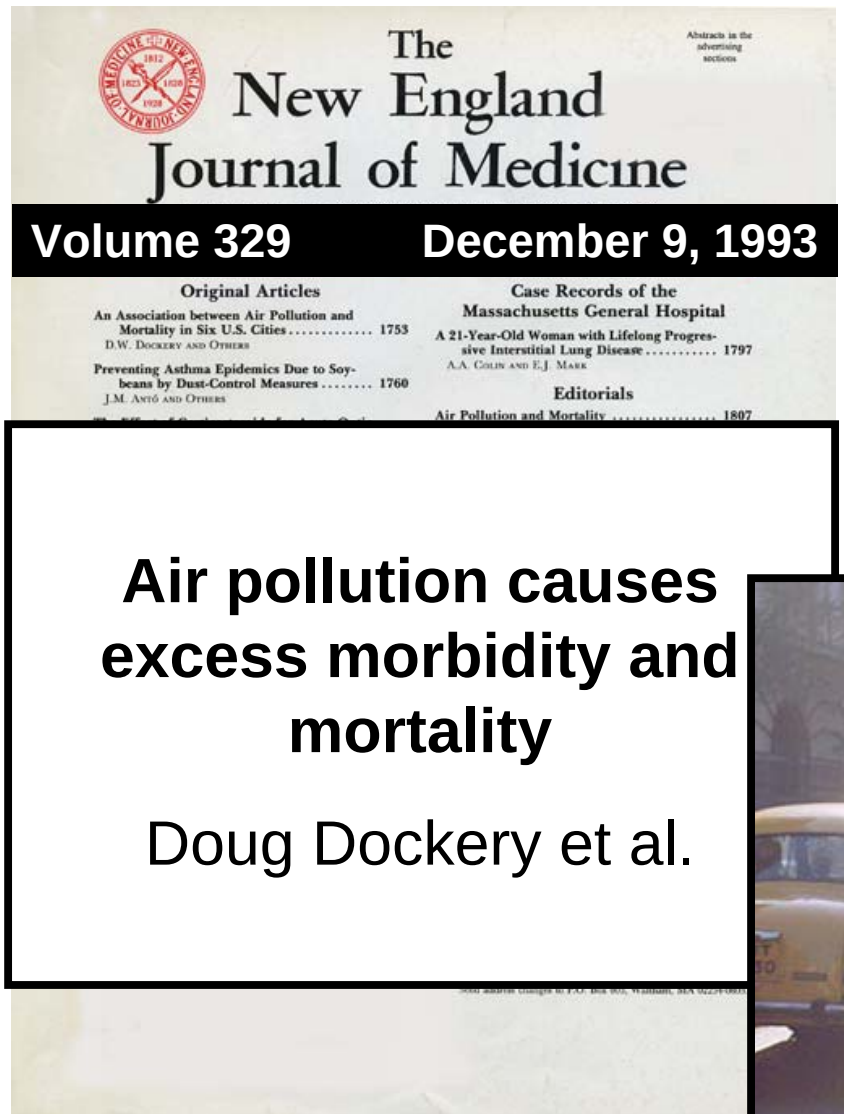
Global Environmental Health

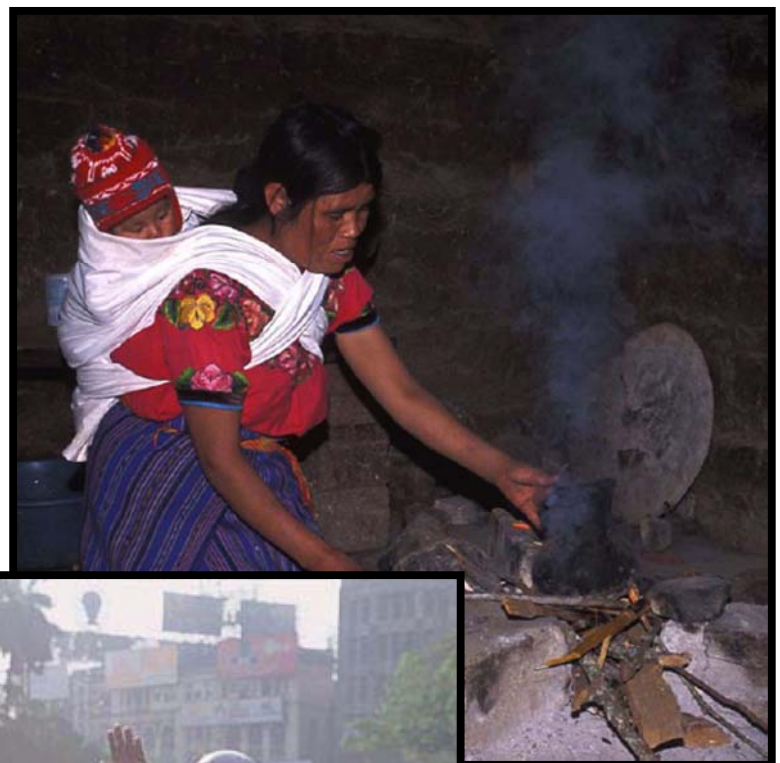


- **Extraordinary exposures represent tremendous research opportunities**
- **Substantial opportunity to have a profound impact on human health and disease**
- **Environmental toxins cross borders and effects can be far-reaching**

Respiratory infections are a major cause of morbidity and mortality among children

Global Environmental Health





Air pollution causes excess morbidity and mortality

Doug Dockery et al.

Priorities for Program Development

- Impact on Human Health and Disease
  - Focus on complex human diseases
  - Support interdisciplinary research
- Environmental Genomics
  - Epigenetics
  - Comparative biology/genomics
  - Training in environmental genomics
- Environmental Biology Program within GEI
- Global Environmental Health